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(54) Abstract Title
ANTIBACTERIAL AGENTS

(57) The use of an effective amount of one or more essential oil(s) selected from coriander, cumin, dill weed, lemongrass and peppermint oil in the manufacture of a composition for the inhibition of pathogenic bacteria present in the oral cavity, the composition being suitable for oral administration.

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Chemical Compositions II

The present invention is concerned with the use of essential oils as antibacterial agents. The present invention is particularly concerned with the use of such oils in the treatment of oral health problems in humans and animals, particularly domestic animals.

It has been suggested that periodontal disease is the single most common disease encountered in small animal veterinary practice. The path to periodontal disease, both in humans and in companion animals, begins with the accumulation of deposits of plaque. Dental plaque is a soft, gelatinous material which forms on a tooth surface and is composed of bacteria and their metabolic by-products, saliva components, food debris and occasional cells from the gums. Plaque deposits are the first step in the development of gingivitis and as such are a significant factor in oral health. Gingivitis is an inflammation of the gums, produced essentially by the body's immune response to the bacteria in dental plaque. Gingivitis sometimes, although not always, leads to the development of periodontal disease.

Halitosis (bad breath or oral malodour) is a common problem both in domestic pets and in humans. Current thinking suggests that the predominant source of bad breath is the mouth. This is supported by experimental findings which show that oral hygiene procedures such as tooth brushing markedly decrease malodour, while conditions such as dental caries and periodontitis increase the incidence and intensity of oral malodour [G.F. Sulser, *et al.* J. Dental Research, 18: 355-359 (1939)]. Oral malodour is produced as a result of microbial metabolism of exogenous and endogenous proteinaceous substrates. No single micro-organism has been indicated as the primary cause. The proteinaceous substrates can be derived from food debris, exfoliated oral epithelium, saliva, blood and gingival crevicular fluid. The proteins obtained from these sources undergo proteolysis to peptides and amino acids which are further metabolised to highly volatile compounds. It is these volatile compounds which are perceived as oral malodour. It has been shown that the predominant unpleasant-smelling components of bad breath are volatile sulphur compounds or VSCs [J. Tonzetich, J. Periodontology, 48: 13-20 (1977)], the most significant being hydrogen sulphide (H_2S) and methyl mercaptan (CH_3SH). The determination of the levels of VSCs

can provide a quantitative measure of the extent of oral malodour and can be used in the evaluation of treatments for reducing oral malodour.

It has been suggested that very many species of bacteria may inhabit the oral cavity, but a subset of these species, most of which are gram negative, anaerobic bacteria, are strongly implicated in periodontitis, oral malodour production and other associated oral health problems (Oral Microbiology, 3rd Edition, P. Marsh and M. Martin (eds), 1992, London, Chapman & Hall). McNamara *et al.* ("The role of microorganisms in the production of oral malodor", Oral Surg, 34(1): 41-48, 1972) proposed that intrinsic oral malodour is readily produced by gram negative micro-organisms in localised areas within the mouth, such as the gingival crevice, interdental spaces, dental plaque, tonsillar folds and papillary crypts of the tongue, where saliva stagnation commonly occurs. It has also been shown that *Streptococcus salivarius*, an aerobic bacteria species, is associated with the functioning of healthy mouths.

It is well known that essential oils have antimicrobial properties and there are many commercial products which exploit these properties, including mouthwashes, shampoos and antiseptic creams. Fornell J. *et al.* (Scand. J. Dent. Res. 1975, 83, 18-25), for example, disclose the plaque-controlling properties of an antiseptic mouthwash comprising thyme and eucalyptus oils. US-5472684 discloses an anti-bacterial oral composition for countering plaque and gingivitis comprising thymol and eugenol.

Deans S.G. and Ritchie G. (Int. J. Food Microbiol., 1987, 5, 165-180) examined the antibacterial properties of fifty essential oils against twenty-five genera of bacteria. In this study, the most comprehensive antibacterial properties where shown by Angelica, Bay, Cinnamon, Clove, Thyme, Bitter Almond, Marjoram, Pimento, Geranium and Lovage essential oils. However, amongst the 25 bacteria species used in that study, 24 were aerobic. Of the essential oils tested, only Angelica, Laurel, Marjoram, Parsley, Pimento, Rosemary and St John's Wort were reported as having any effect on the anaerobic species.

The antimicrobial activity of various essential oils has also been documented by Morris, J.A. *et al.* (J. Am. Oil Chem. Soc. 1979, 56, 595-603). In that study, essential oils such as clove and lemongrass oils demonstrated good antibacterial activity against aerobic

bacteria. Further investigations on the antimicrobial activity of various essential oils were conducted by Youssef R.T. and Tawil G.G. (Pharmazie 35, H.11 1980) and by Balchin *et al.* (Flavour and Fragrance Journal, 13, 98-104, 1998; and J. Herbs, Spices & Med. Plants, 4(2), 69-86, 1996).

It is an object of this invention to provide an antibacterial agent which exhibits antibacterial activity against pathogenic bacteria present in the oral cavity of humans and other mammals. It is a further object of this invention to provide an antibacterial agent which exhibits antibacterial activity against anaerobic bacteria present in the oral cavity of humans and other mammals. It is a further object of this invention to provide an antibacterial agent which exhibits antibacterial activity against gram negative, anaerobic bacteria present in the oral cavity of humans and other mammals.

It has now been found that certain essential oils, which in earlier studies had previously demonstrated only weak antibacterial activity, are particularly potent in their antibacterial effect against species of bacteria which are strongly implicated in periodontal disease and/or malodour production.

According to the present invention there is provided the use of an effective amount of one or more essential oils selected from coriander oil, cumin oil, dill weed oil, lemongrass oil and peppermint oil in the manufacture of a composition for the inhibition of pathogenic bacteria, particularly anaerobic bacteria, present in the oral cavity of humans and other mammals, the composition being suitable for oral administration.

According to a further aspect of the invention there is provided a method of inhibition of pathogenic bacteria, particularly anaerobic bacteria, present in the oral cavity of humans and other mammals, by the oral administration to a subject in need thereof of a composition comprising an effective amount of one or more essential oil(s) selected from coriander, cumin, dill weed, lemongrass and peppermint oils.

The use or method of the present invention is directed to the maintenance of oral health. The use or method may be used in the treatment of halitosis or disorders associated with

the oral cavity, particularly such disorders which are related to or substantially caused by the activity of anaerobic bacteria.

As used herein, the term "disorders associated with the oral cavity" refers to gingivitis, periodontal disease and dental caries.

The use or method of the present invention is intended for use in both humans and animals, particularly domestic animals.

An essential oil is the volatile ethereal fraction obtained from a plant or plant part by a physical separation method. The physical separation method usually involves either distillation (including water distillation, steam distillation, water and steam distillation and dry distillation) or expression (pressing). Enfleurage, a process in which a floral material is adsorbed onto fat and the essential oil obtained by alcoholic extraction from this fat, may also be used to obtain the essential oil. Generally, essential oils represent the odorous part of the plant material.

The essential oils are either available commercially or may be obtained from the plant or plant part by conventional separation techniques, as described above.

In one embodiment, the composition comprises at least about 5 ppm, preferably at least about 50 ppm, preferably at least about 100 ppm, more preferably at least about 150 ppm and more preferably at least about 200 ppm by weight of the composition of the or each essential oil. It is preferred that the composition comprises no more than about 20000 ppm, preferably no more than about 10000 ppm, preferably no more than about 5000 ppm, preferably no more that about 2000 ppm, preferably no more that about 1000 ppm, and preferably no more than about 500 ppm by weight of the composition of the or each essential oil.

In general, compositions for animal use contain a smaller amount of active ingredient in relation to compositions for human use. If too great an amount of active ingredient is added, the composition becomes unpalatable for the animal. Preferably, compositions for animal use contain no more than about 2000 ppm, preferably no more than about 1000

ppm, and preferably no more than about 500 ppm by weight of the composition of the or each essential oil.

According to a further aspect of the invention, there is provided a composition for the inhibition of pathogenic bacteria, particularly anaerobic bacteria, present in the oral cavity of humans and other mammals, the composition being suitable for oral administration and comprising an effective amount of one or more essential oil(s) selected from cumin oil, coriander oil, dill weed oil, lemongrass oil and peppermint oil.

According to a further aspect of the invention there is provided a process for the production of a composition for the inhibition of pathogenic bacteria, particularly anaerobic bacteria, present in the oral cavity of humans and other mammals, the composition being suitable for oral administration, as herein described, the process comprising the steps of admixing an effective amount of one or more essential oil(s) selected from cumin oil, coriander oil, dill weed oil, lemongrass oil and peppermint oil with one or more conventional and acceptable carriers or excipients. In an alternative embodiment, such as the embodiment relating to chewable animal products described below, the one or more essential oil(s) selected from cumin oil, coriander oil, dill weed oil, lemongrass oil and peppermint oil are applied to the surface of a conventional carrier composition such as a rawhide strip.

Suitable formulations for the use and method of treatment of the present invention will now be described for animal and human subjects.

In the aspect of the invention which is directed to the use or method described herein in relation to animals, particularly domestic animals, the compositions can be any of the conventional animal food types known in the art, including dry pet foods such as pelletized dog or cat foods or main meals, etc. Alternatively, the active ingredient(s) may be incorporated into a composition which is a chewable product or toy, such as a chewable plastic product or toy, or a rawhide chew.

It is preferred that a pet food composition is a dry or semi-moist pet food, preferably a biscuit. In addition to the essential oil(s), the compositions may comprise ingredients and

additives similar to those used in conventional pet foods. The essential oil(s) may be added to the pet food composition at any stage of its manufacture. The pet food compositions may be made according to conventional methods well-known to those skilled in the art. The manufacture of dry and semi-moist pet foods and particularly pet biscuits generally involves the step of shaping and baking a dough containing the desired ingredients. The dough can be any suitable dough known in the art. The essential oil(s) are generally added to the dough before baking and, accordingly, if the essential oil is volatile the dough should contain a higher concentration of essential oil than is desired in the final biscuit. Typically, the dough should contain the essential oil(s) in an amount which is between 2 and 10 times greater than that required in the final biscuit. The precise amount of essential oil(s) added to the dough will depend, *inter alia*, on the temperature and duration of heating, on the size of the biscuit and on the volatility of the plant extract(s) used.

In one embodiment, the term "dry pet food" as used herein is intended to mean a pet food having a water activity A_w of less than 0.65. In this embodiment, the term "semi-moist pet food" as used herein is intended to mean a pet food having a water activity A_w of from about 0.65 to about 0.86. Water activity is a measure of the relative humidity above a sample of the pet food. The relative humidity is measured above a sample in a sealed chamber after being allowed to equilibrate. A device which is suitable for measuring these parameters is the Rotronic Hygroskop DT™. The water activity is on a scale of 0 to 1.0 and is defined as:

$$\text{water activity } A_w = {}^{1}/_{100} \text{ (relative humidity)}$$

The water activity reflects the amount of water which is available to micro-organisms for growth and multiplication. At a water activity of less than 0.65, it is not usually necessary to add preservatives to the pet food. At a water activity of from about 0.65 to about 0.86, it is desirable to add preservatives to the pet food to prevent the growth of mould although the growth of bacteria is minimal under such conditions.

The water content that corresponds to the water activities defined above can vary considerably depending upon a number of factors, such as the presence and levels of humectants (such as salt, sugar or glycerol etc) in the pet food. Typically, however, a "dry

pet food" has a water content of less than about 15% by weight of the final biscuit and a "semi-moist pet food" has a water content of from about 15% to about 25% by weight of the final biscuit. Thus, in an alternative embodiment, the term "dry pet food" as used herein means a pet food which has a water content of less than about 15%, preferably less than about 14%, by weight of the final biscuit. In this alternative embodiment, the term "semi-moist pet food" as used herein means a pet food which has a water content of from about 15% to 25%, preferably from about 14% to about 25%, by weight of the final biscuit.

The preparation of dog biscuits will now be described in detail.

The dog biscuits can be made from conventional dog biscuit doughs. The dough can comprise at least one flour, meal, fat and water. A conventional dough for dog biscuits may also contain discrete particles of meat and/or meat byproducts or farinaceous material. Such doughs typically contain fat solids. Examples of suitable doughs for the production of hard dog biscuits are disclosed in U.S. Patent Nos. 4,454,163 and 4,743,459, and suitable doughs for the production of soft dog biscuits (containing humectant to control water activity) are disclosed in U.S. Patent No. 4,454,164. The disclosures of such doughs and the manufacture of pet food disclosed in U.S. Patent Nos. 4,454,163, 4,454,164 and 4,743,459 are incorporated herein by reference. Particulate proteinaceous particles, such as particles of meat, texturized vegetable protein and/or meat byproducts, can be incorporated to add flavour to the biscuits and texturize the surface. (See U.S. Patent 4,743,459, for example.) Particular farinaceous materials, such as bran particles, can also be employed to texturize the interior and/or surface or the biscuits and to provide other useful properties to the product. A dough found to produce biscuits highly palatable to dogs includes suitable proportions of wheat flour, wheat meal, soybean meal, meat and bone meal, animal fat and natural flavours in admixture with water. The meal used in the doughs suitable for production of biscuits of the invention can comprise meat and/or bone and/or vegetable matter including farinaceous materials, materials prepared from legumes such as beans and peas, tuberous materials such as potato meal, and the like. The meals can be finely or coarsely ground as desired for the texture. Flours made from any suitable farinaceous material can be used.

A suitable dough contains farinaceous material, an edible oil, an antioxidant, an antimycotic, salt, animal fat added vitamins and minerals, such as those disclosed in U.S. Patent No. 4,229,485, column 5, lines 7 to 57, which is incorporated herein by reference. The compositions of the invention may also contain at least one animal-derived proteinaceous meal such as meat meal, bone meal or fish meal. A good biscuit dough for producing the biscuits of the invention contains about 50 to 60 percent by weight of wheat flour, about 5 to 10 percent by weight of soybean meal, about 3 to 10 percent by weight of meat and bone meal, about 1 to 5 percent of wheat meal, about 1 to 5 percent of animal fat preserved with BHA, about 20 to 30 percent by weight of water, about 2 to 5 percent by weight of natural flavours, vitamin and mineral preblend, and acidulant.

The dough ingredients are generally admixed at a temperature of about 5° to about 60° C, preferably about 15°C to about 30°C.

The dog biscuit doughs can contain a softening agent or humectant. The preferred humectant is propylene glycol. Examples of other humectants which can be used are corn syrup, sugar and polyalcohols, such as sorbitol and glycerin.

The dough can also contain edible surfactants or emulsifying agents, e.g. cationic agents and nonionic agents. Exemplary nonionic emulsifying agents can be broadly defined as compounds produced by the condensation of alkylene oxide groups (hydrophilic in nature) with an organic hydrophobic compound which can be aliphatic, alkyl aromatic, or a condensate of an alkylene oxide with an alkylene glycol (hydrophilic in nature). Examples of nonionic emulsifying agents which can be used include polyethylene oxide condensates of alkyl phenols, products derived from the condensation of ethylene oxide with the reaction product of propylene oxide and ethylene diamine, ethylene oxide condensates of aliphatic alcohols, long chain tertiary amine oxides, long chain tertiary phosphine oxides, long chain dialkyl sulfoxides and mixture of such materials. The emulsifier is generally used in minor amounts.

The dog biscuit dough can be mixed using conventional equipment. For example, the mixing can be at 20 to 100 rpm. For example, a dry blending step can be done at room temperature for a period of time of about 3 minutes to about 20 minutes. The dry-blended

mixture can then be mixed with water to form a first stage dough. The water which can be admixed with the dryblended mixture is typically at a temperature of about 20°C to about 65°C. The water can be added, with mixing, over a period of time of about 3 minutes to about 6 minutes to form the first stage dough. Then, the fat portion of the biscuit dough can be admixed with the first stage dough to form the final stage dough. The fat portion can be added at a temperature at which it is at least fluid, typically at about 35°C to about 65°C. The fat portion can be mixed for a period of time which is sufficient to form a dough whose homogeneity is visually apparent. A typical final mixing time is about 3 to about 5 minutes.

Formation of the dough is achieved at about atmospheric pressure with the mixing of the components being conveniently achieved in an upright sigma blade mixer or other bakery-type mixers. The various ingredients can be added over a period of time or in a one-shot process according to the above order of addition. However, melted fat and water can be added simultaneously and mixed for about 6 to 10 minutes.

The dog biscuits are formed in any conventional or suitable manner, such as by extrusion, stamping, cutting or molding. Any suitable dog biscuit shape, such as a bone-shaped biscuit, can be used. For many products, such as the bone-shaped canine biscuits of the invention, a rotary molding system is preferred because it permits the rapid forming of dough pieces with good control over their shape, form and surface characteristics. Docker holes are optionally formed in the dough piece during molding to facilitate the escape of moisture during baking, cooking and/or drying.

The dough is formed into pieces by machining on a rotary molder with specific die shapes. The dough can also be formed into pieces by sheeting followed by either a vertical or rotary cutter or by a rotary molder. Suitable die and cutter shapes are those which result in biscuit products having bone, round, square, triangular, T-bone or chop shapes and the like. The forming is achieved at conventional temperatures of ambient to about 45°C and pressures of less than about 5½ kg/cm^2, used with a rotary molder, a vertical cutter or rotary cutter.

The dough pieces can be baked using any suitable or conventional equipment and conditions. For example, the dough pieces can be passed into a conventional oven where the biscuit is baked. The conveyer belts of the oven can be coated with an edible lubricant, such as a natural or synthetic cooking oil or shortening, to facilitate separation of the conveyer belts of the baked product. Temperatures in the range of about 100°C to about 300°C can be used. The baked biscuits can also be subjected to subsequent drying at temperatures of about 90°C to 200°C either within the baking oven or separately, to produce the desired moisture content in the final product. Baking and drying temperatures and times are those conventionally used in the production of a canine biscuit. Typically, baking temperatures and times for a hard, dry canine biscuit are about 100°C to about 250°C for about 25 minutes to about 8 minutes. Drying conditions for a hard, dry canine biscuit are typically about 90°C to about 160°C for about 25 minutes to about 12 minutes in a forced air dryer. On a weight basis, the moisture content of the final dry biscuit is preferably less than or equal to about 15 percent by weight and preferably about 10 to 12 percent by weight of the final biscuit at 70 percent relative humidity.

The baking and drying process provides a shelf stable product without the need of any moisture barrier protection.

The pet food composition is particularly of use for dogs. For an average biscuit weight of 10 grams, a recommended maximum biscuit intake is about 10 biscuits a day for a medium size dog, which should supply, for example, about 1/4 of the daily calorific requirement of a 25 kg dog.

Chewable products and rawhide chews are well-known in the art. For instance, EP-A-0272968 discloses a chewable product for dogs and other domestic animals wherein aqueous solutions of oral care agents, such as sodium flouride (an anti-caries agent), sodium benzoate (an anti-calculus agent) and bromochlorophene (an anti-microbial/anti-plaque agent), are used to soak rawhide, beef tendon or ligament. The solution-treated product is then dried and the oral care agents are absorbed into the surface of the product. The disclosure of EP-A-0272968 relating to the manufacturing process for chewable products, particularly rawhide chews, is incorporated herein by reference. Other animal chew products are disclosed in US-5405836 and EP-A-0552897.

A rawhide chew for use in the present invention may be any of those commercially available or may be made according to any of the processes known in the art. Usually, rawhide chews are elongated strips of treated rawhide, which may be knotted, although any shape of rawhide chew may be used in the present invention. The active ingredients may be applied topically to the rawhide, for example by spraying or dipping, using an aqueous solution. Conventional spraying or dipping equipment may be used. The aqueous solution may contain a fat, such as tallow, which may improve the adhesion of the solution and active ingredient to the chew. The fat content of the solution may, for example, be up to 10 % by weight, preferably from about 0.2 to about 3 % by weight. The animal may chew from 1 to about 3 pieces of rawhide chew per day to achieve the desirable anti-bacterial effects described herein.

With regard to human subjects, the compositions may be incorporated into oral formulations in general, such as mouthrinses, toothpastes, lozenges, confectionery, chewing gum or dental floss, containing a dental vehicle.

The dental vehicle contains liquids and solids in a dentifrice. In general, the liquid comprises water and/or a humectant, such as glycerine, sorbitol, polyethylene glycol or propylene glycol including suitable mixtures thereof. It is usually advantageous to use a mixture of both water and one or more humectants. The total liquid content is generally about 5-90 percent by weight of the vehicle. In transparent and translucent vehicles, the liquid content of a toothpaste may be about 5-90 percent by weight, while in opaque vehicles the total liquid content is usually about 5-50 percent by weight. Preferred humectants are glycerine, sorbitol, and polyethylene glycol.

The solid portion of the vehicle is a gelling agent. In the instant invention, the gelling agent includes alkali metal carboxymethyl cellulose, hydroxyethyl cellulose and hydroxymethyl cellulose in an amount of at least about 0.5 percent by weight of the vehicle. Additional gelling agents may also be present. Gelling agents which may be additionally present include xanthan gum, viscarin, gelatin, starch, glucose, sucrose, polyvinyl pyrrolidone, polyvinyl alcohol, gum tragacanth, gum karaya, hydroxypropyl cellulose, methyl cellulose, carboxyethyl cellulose (CMC) and sodium alginate. The solid

portion or gelling agent of the vehicle is typically present in an amount of about 0.5-5.0 percent by weight of the toothpaste and preferably about 0.5-2.0 percent by weight.

Any suitable substantially water-insoluble polishing agent may be added to the gel vehicle of the dentifrice. There is a relatively large number of such materials known in the art. Representative materials include, for example, dicalcium phosphate, tricalcium phosphate, aluminium hydroxide, magnesium carbonate, calcium carbonate, calcium pyrophosphate, calcium sulfate, bentonite, alumina, hydrated alumina, aluminum silicate, zirconium silicate and silica, including mixtures thereof.

Water-soluble polishing agents, such as sodium bicarbonate can also be used. When sodium bicarbonate is present, plaque and caries reduction is generally improved.

In general these polishing agents will comprise a major proportion by weight of the solid ingredients. The polishing agent content is variable but will generally be up to about 75 percent by weight of the total composition, preferably about 20-75 percent, although even lower amounts of polishing agent can be employed, for instance about 10% or more of sodium bicarbonate.

Any suitable surface-active material may be incorporated into the gel vehicle. Such compatible materials are desirable to provide detersive and foaming properties depending upon the specific type of surface-active material selected. These detergents are water-soluble organic compounds for the most part and may be anionic, cationic or non-ionic in structure. It is preferred to use the water-soluble non-soap or synthetic organic detergents. Suitable detersive materials are known and include the water-soluble anionic salts of higher fatty acid monoglyceride monosulfate detergents (e.g., sodium coconut fatty acid monoglyceride monosulfate), higher alkyl sulfates (e.g., sodium lauryl sulfate), alkyl aryl sulfonates (e.g., sodium dodecyl benzene sulfonate), higher fatty acid esters of 1,2-dihydroxypropane sulfonate, and the like. Other suitable surface-active materials include non-ionic surface-active agents, such as condensates of ethylene oxide with propylene oxide condensates of propylene glycol.

The various surface-active materials may be used in any suitable amount, generally from about 0.05 to about 10 percent by weight, and preferably from about 0.5 to about 5 percent by weight of the dentifrice composition.

The compositions may also contain antiplaque activity boosters in minimal amounts up to about 5 percent by weight, such as polyvinyl maleic acid/maleic anhydride copolymer or polyvinyl phosphonate which deposits on tooth surfaces and inhibits plaque adhesion onto the surface. The essential oils work by a different mechanism; as antimicrobials they inhibit bacterial reproduction and hence plaque growth. Therefore, the two different mechanisms for fighting plaque are complimentary and additive.

The compositions may also contain conventional ingredients, such as colouring or whitening agents (e.g. titanium dioxide), flavouring and/or sweetening materials, fluorides, such as sodium fluoride, stannous fluoride and sodium monofluorophosphate, and the like. These additional ingredients may each be added to the dentifrice in minimal amounts of up to 5 percent by weight and preferably up to about 1 percent, with respect to compounds which do not contain fluorine, and with respect to compounds which do contain fluorine, amounts to provide about 100 to about 10,000 ppm fluoride, preferably about 500 to about 2,000 ppm, provided that they do not interfere with the antiplaque properties of the finished product.

The composition may also be a liquid, such as mouthrinse which typically contains about 60-99 percent by weight of an aqueous non-toxic lower aliphatic alcohol, preferably having about 5-30 percent by weight of a non-toxic alcohol, such as ethanol, n-propanol or isopropanol, with water and often about 5-35 percent of humectant.

Such oral preparations are typically applied by contacting natural or artificial teeth and gums through brushing with a dentifrice or toothpaste or by contacting teeth and gums by rinsing the oral cavity for about 15-90 seconds, or in the case where lozenges, candy or chewing gum are used by sucking or chewing in the oral cavity, or in the case of a mouthspray by spraying the oral surfaces at least once daily.

The invention will now be described with reference to the following examples. It will be appreciated that what follows is by way of example only and that modification of detail may be made without departing from the scope of the invention.

EXPERIMENTAL

Activity against selected oral bacteria

Antimicrobial activity was tested using axemic cultures of oral bacteria (see Table 1) grown *in vitro*. All oral isolates were of human origin. The organisms were chosen on the basis of their roles in the development of halitosis and/or periodontal disease (chronic and acute), as documented in the literature. Sunflower oil and olive oil were included as negative controls.

Table 1

Identity	**Bacterial Accession Numbers**	**Role in halitosis**	**Role in Chronic periodontitis[1]**	**Role in acute necrotising gingivitis[1]**
Prevotella oralis	NCTC 11459	Yes	No	No
Prevotella melaninogenica	NCTC 11321	Yes	No	No
Porphyromonas gingivalis	NCTC 11834	Yes	Yes	Yes
Fusobacterium nucleatum	NCTC 10562	Via disease	Yes	Yes
Peptostreptococcus anaerobius	NCTC 11460	Yes	Yes	No
Veillonella alcalescens	NCTC11809	Via disease	No	No

[1] Marsh P. and Martin M. (Eds), 1992, Oral Microbiology, 3rd Ed, Chapman and Hall, London.

Determination of antimicrobial activity was based on the method of Bennet *at al.* (Applied Microbiol, 1966, 14, 170-177). Pure cultures of each organism were grown overnight in Iso-Sensitest broth, 37°C (Balchin *et al.*, Flavour and Fragrance J., 1998, 13, 98-104)). 10 ml of each culture was transferred to 250 ml sterile molten Iso-Sensitest agar at 45°C

(Deans and Ritchie, Int. J. Food Microbiol., 1987, 5, 165-180)), mixed using a magnetic stirrer and transferred to sterile 90 mm diameter petri plates. After setting, an agar punch (Pharmacia) was used to produce wells (4 mm diameter) in the agar surface. After use on each plate, the tip of the punch was disinfected using an ethanol wipe. The test oil was filter-sterilised prior to use (Whatman polydisc filter 0.2 μm) and 10 μl of oil was pipetted into each well in the agar surface. A maximum of 4 wells were produced on each plate in order to help prevent vapour pressure increases affecting growth. The plates were individually sealed using nonporous plastic tape (Nescofilm) to prevent drying along the edge of the agar. Plates were incubated for 48 h, upright in anaerobic jars at 25°C. Zones of inhibition were measured using vernier callipers (Philip Harris Scientific) to the nearest 0.1 mm through the back of the plate. Duplicate plates were prepared for each sample mix and the experiment was repeated twice.

All culture media were supplied by Oxoid Limited, UK, except where indicated. Sunflower and olive oils were purchased from Sainsbury's Plc. Essential oils were obtained from H. E. Daniel Limited, Billingham, UK.

The results of the experiments are displayed in Table 2. Antibacterial activity was graded as low (0-5.0 mm inhibition zone), medium (5.1-10.0 mm) or high (>10.0 mm). Coriander, cumin, dill weed, lemongrass and peppermint oils exhibited high antibacterial activity against at least four of the test organisms. Sunflower and olive oil showed little or no effect on bacterial viability.

Table 2

	Zone of Inhibition (mm) ± SD (n=4)					
Sample	*Prevotella oralis*	*Prevotella melaninogenica*	*Porphyromonas gingivalis*	*Fusobacterium nucleatum*	*Peptostreptococcus anaerobius*	*Veillonella alcalescens*
Coriander	5.0 ± 1.8	12.0 ± 2.7	12.5 ± 1.8	>20.0 ± 0.0	19.5 ± 0.5	0.0 ± 0.0
Cumin	0.0 ± 0.0	16.0 ± 2.6	10.5 ± 1.5	>20.0 ± 0.0	18.5 ± 1.6	3.0 ± 2.1
Dill weed	0.0 ± 0.0	20.0 ± 1.5	1.5 ± 0.5	>20.0 ± 0.0	20.0 ± 1.8	18.0 ± 5.0
Lemongrass	9.0 ± 1.1	12.0 ± 2.3	5.0 ± 1.0	>20.0 ± 0.0	>20.0 ± 0.0	19.0 ± 0.9
Peppermint	11.0 ± 2.9	12.5 ± 2.2	0.0 ± 0.0	>20.0 ± 0.0	16.5 ± 4.8	5.0 ± 0.6
Sunflower	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	1.0 ± 0.5	0.0 ± 0.0	0.0 ± 0.0
Olive	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.5 ± 0.1	0.0 ± 0.0	0.0 ± 0.0

Example

A dog biscuit was prepared according to conventional techniques using 0.1% cumin oil and a biscuit dough comprising the following ingredients:

Ground Wheat	30%
Oats & Bran	17.5%
Grits & Seeds	16.5%
Gluten	7.5%
Sugar	6%
Fat	5%
Aromas, Flavours	7.5%
Vitamins & Minerals	10%

The cumin oil was added to the biscuit dough prior to forming and baking.

Claims

1. The use of an effective amount of one or more essential oil(s) selected from coriander, cumin, dill weed, lemongrass and peppermint oil in the manufacture of a composition for the inhibition of pathogenic bacteria present in the oral cavity, the composition being suitable for oral administration.

2. A method for the inhibition of pathogenic bacteria present in the oral cavity by the oral administration to a subject in need thereof of a composition comprising an effective amount of one or more essential oil(s) selected from coriander, cumin, dill weed, lemongrass and peppermint oil.

3. The use or method according to claim 1 or 2 wherein said use or method is for the maintenance of oral health.

4. The use or method according to claim 1, 2 or 3 wherein said use or method is for the inhibition of anaerobic bacteria.

5. The use or method of any of claims 1 to 4 wherein the composition is for the treatment of disorders associated with the oral cavity.

6. A use or method according to claim 5 wherein said disorders associated with the oral cavity are one or more of gingivitis, periodontal disease and dental caries.

7. The use or method of any of claims 1 to 4 wherein the composition is for the treatment of halitosis.

8. The use or method of any of claims 1 to 7 wherein the composition is for administration to humans.

9. The use or method of any of claims 1 to 7 wherein the composition is for administration to animals.

10. A use or method according to claim 9 wherein said composition is a dry or semi-moist pet food.

11. A use or method according to any preceding claim wherein the essential oil is cumin oil.

12. A use or method according to any preceding claim wherein the amount of the or each essential oil is at least about 50 ppm by weight of the composition.

13. A use or method according to any preceding claim wherein the amount of the or each essential oil is no more than about 20000 ppm by weight of the composition.

Application No: GB 0000187.5
Claims searched: 1-13

Examiner: Dr Paul D Jenkins
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Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.R): A2B (BAAC, BMA9); A5B (BFA)

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Other: Online: AGRICOLA, CAS-ONLINE, EPODOC, FROSTI, FSTA, JAPIO, KOSMET, WPI

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X	EP 0473171 A1	(KAO CORPORATION) - see especially claim 1 and example 1	1-13
X	WO 99/27793 A2	(BARRIER BIOTECH) - see especially claim 1 and page 3, lines 3-7	1-13
X	WO 97/16159 A1	(WARNER-LAMBERT) - see especially page 1, line 13 to page 2, line 3 and page 4, lines 13-29	1-13
X	WPI Abstract AN 1996-055909 [07] & JP 070316064 (MORISHITA) - see abstract		1-13
X	WPI Abstract AN 1984-078372 [25] & JP 590029620 (HASEGAWA) - see abstract		1-13
X	WPI Abstract AN 1984-053797 [09] & JP 590013712 (LION) - see abstract		1-13

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.